

Remarks

Claims 1-31 are pending. Claims 11-19, 21-27, 30 and 31 are withdrawn. Claims 1-10, 20 and 28-29 are rejected. Claims 1, 3, 4, 6, 7, 28 and 29 are currently amended. Claims 32 and 33 are new. Paragraph [0039] has been amended merely to correct the date in a citation. Support for the amendments and the new claims can be found at, for example, paragraphs [0022], [0031]-[0048], [0052]-[0066], [0068]-[0069], [0071], [0072], [0074], [0081] and [0084], Example 1 from which one of ordinary skill in the art would recognize the methods disclosed are performed on a particular machine, namely at least one specifically programmed computer (e.g. in a network such as the internet) which can display the identified combinations of motifs. Additionally, certain of the amendments are merely made for the sake of clarity.

At the outset, the Applicants wish to thank the Examiner for the helpful interview of February 3, 2009 in which the rejections under 35 USC §101, 35 USC §112 and 35 USC §103, as well as the objections, were discussed. The Applicants note that the amendments in the Response are consistent with the helpful guidance provided by the Examiner both during the interview and in the Official Action.

Claim 4 was objected to for reciting “wild sequence[.]” Claim 4 has been amended to recite a “wild-type sequence[.]” This is consistent with the Examiner’s helpful guidance. Withdrawal of the objection to Claim 4 is respectfully requested.

Claim 6 was objected to for the absence of a comma after the term “matrices[.]” Claim 6 has been amended to recite “matrices,” as suggested by the Examiner. Withdrawal of the objection to Claim 6 is respectfully requested.

Claims 1-10, 20 and 28-29 are rejected under 35 USC §101 as being directed to non-statutory subject matter.

Claims 1-10, 20 and 28-29 are directed to statutory subject matter under 35 USC §101. Reasons are set forth below.

Claim 1 has been amended to recite the steps of “a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a multiple sequence alignment program” and “d) outputting the identified motifs to a computer controlled display” and stipulates that “the steps of the method are performed on a programmed computer.” Claims 3-10, 21, 29 and 30 are dependent on independent Claim 1 and incorporate all of its recitations.

This means that the claimed methods are tied to a particular machine and are limited to operation on at least one specifically programmed computer. Such a specifically programmed computer is a particular machine by virtue of the fact that the microchips and memory components of this machine have been specifically configured, upon programming, to comprise unique circuits, switches, and physical states (*e.g.* specific hysteresis states for the machine's physical storage media such as a magnetic hard drive or specific switch configurations for other types of storage media).

This is apparent from the recitation of step "a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a multiple sequence alignment program" in the claimed methods. As exemplified at paragraphs [0036]-[0048] such multiple sequence alignment programs can be based on, for example, the CLUSTAL W algorithm or a Hidden Markov Model, but can also be performed by means of other alignment methods known in the art.

Additionally, the recitation of step "d) outputting the identified motifs to a computer controlled display" also imposes meaningful limits on the scope the claims. In fact, claims containing similar limitations have previously been held to be directed to patentable subject matter under 35 USC §101 in a number of different cases including at least one of the cases cited in the rejection. *See e.g. Diamond v. Diehr*, 450 US 175 (1981) (cited in the rejection); *see also In re Abele*, 684 F.2d 902 (CCPA 1982); and *In re Bilski*, 2008 U.S. App. Lexis 3246, 49-50 (Fed. Cir. 2008) (discussing *In re Abele* and acknowledging that a process using a computer implemented algorithm and reciting a computer controlled display step recites patentable subject matter under 35 USC §101).

Furthermore, the recent decision of *In re Bilski* made it clear that such claims are directed to patentable subject matter under 35 USC §101. This point was made explicit when that Court stated:

We further note for clarity that the electronic transformation of the data itself into a visual depiction in *Abele* was sufficient; the claim was not required to involve any transformation of the underlying physical object that the data represented. We believe this is faithful to the concern the Supreme Court articulated as the basis for the machine-or-transformation test, namely the prevention of pre-emption of fundamental principles. So long as the claimed process is limited to a practical application of a fundamental principle to transform specific data, and the

claim is limited to a visual depiction that represents specific physical objects or substances, there is no danger that the scope of the claim would wholly pre-empt all uses of the principle.

See In re Bilski, 2008 U.S. App. Lexis 3246, *50 (Fed. Cir. 2008) (discussing In re Abele).

The specification also states “[t]he method of the invention also makes it possible to construct a database which constitutes a decision-making tool[.]” See e.g. paragraph [0077] of the originally filed application (emphasis added). Importantly, such construction necessarily requires a physical transformation and one of ordinary skill in the art would recognize that a “database” in the context of the application is a computer database. In fact, this is consistent with a reasonable interpretation of the term “database” in the context of the application to mean “any electronically-stored collection of data.” See e.g. Alan Freedman, The Computer Glossary 90 (8th Ed. 1998). One of ordinary skill in the art would also recognize that the matrices constructed in the steps of the method represent databases because the data in matrices must be stored electronically if they are to be used in the other steps of the claimed methods. Furthermore, Example 1 clearly shows the output from the claimed methods to a computer controlled display such as a computer controlled display screen or computer controlled printer.

Stated differently, the foregoing makes it clear that the amended claims are tailored narrowly enough to encompass only particular applications of the methods, rather than pre-empting substantially all uses of the principle embodied by the methods and are not directed to mental processes, phenomena of nature or abstract intellectual concepts. This means the claimed methods are directed to patentable subject matter.

Last, the US Supreme Court’s decision in Diamond v. Chakrabarty clearly stated that patentable subject matter under 35 USC §101 “includes anything under the sun that is made by man” and noted that the subject matter included within the scope of 35 USC §101 includes “process[es.]” See Diamond v. Chakrabarty, 447 US 303, 309 (1980). Most importantly, the rules articulated by the US Supreme Court’s decision in this case is binding legal precedent and cannot simply be overturned by the decision of a lower court such as a court of appeals (e.g. the US Federal Circuit Court of Appeals).

The Applicants respectfully request withdrawal of the rejections of Claims 1, 3-10, 21, 29 and 30 under 35 USC §101.

Claim 1 is rejected under 35 USC §112, second paragraph, as indefinite.

Claim 1 is definite under 35 USC §112, second paragraph. This is because Claim 1 has been amended to remove the phrase “physically transforming the identified motifs” such that the rejection is now obviated.

The Applicants respectfully request the withdrawal of the rejection of Claim 1 under 35 USC §112, second paragraph.

Claims 1-10, 20 and 28-29 are rejected under 35 USC §112, first paragraph, as containing new matter.

Claims 1-10, 20 and 28-29 do not contain new matter under 35 USC §112, first paragraph. Reasons are set forth below.

Claim 1 has been amended to recite the step of “d) outputting the identified motifs to a computer controlled display[.]” Claims 3-10, 21 and 29 are dependent on independent Claim 1 and incorporate all of its recitations.

As a preliminary matter, the Applicants wish to note that the language in step d) was originally proposed by the Examiner in the Official Action mailed August 6, 2008. Thus, it appears the Examiner himself correctly recognized that the language of step d) is not new matter.

Additionally, one of ordinary skill in the art would recognize that the originally filed application discloses “outputting the identified motifs to a computer controlled display[.]” This is because it is apparent from the specification that the claimed methods may be performed by at least one specifically programmed computer.

For example, in the working example, a multiple sequence alignment matrix is generated. The specification teaches that the data for such multiple sequence alignments can be obtained from a computer databank using websites such as that of the Los Alamos library. *See e.g.* paragraphs [0014], [0035], [0036], [0043], [0059], [0071], [0080] and [0084] of the originally filed application. This necessarily must be done by the use of at least one specifically programmed computer. Additionally, one of ordinary skill in the art would recognize that amino acid sequence data for proteins and nucleotide sequence data for nucleic acids is routinely used in computer readable formats and also displayed using computers. The well known FASTA format is one example of such a computer readable format. The computer readable ASCII text file provided as part of the sequence listing with this, and other US patent applications, is another example.

The specification teaches that a CLUSTAL based computer algorithm, such as the CLUSTAL W computer algorithm, or a Hidden Markov Model based computer algorithm can be used to generate these alignments using a databank. *See e.g.* paragraphs [0037]-[0048] of the originally filed application. Importantly, those of ordinary skill in the art will recognize that such algorithms are implemented with “a programmed computer using a multiple sequence alignment program[(*e.g.* CLUSTAL W).]” The specification also teaches that the number of sequences to be aligned can be greater than 100 (*e.g.* 24,115 sequences) which one of ordinary skill in the art would recognize must be done using a computer. *See e.g.* paragraphs [0038]-[0040] of the originally filed application. In fact, the Collins reference cited by the Examiner underscores this point as it is solely devoted to database searching and alignments. Additionally, one of ordinary skill in the art would recognize the analysis of matrices representing datasets containing information derived from an alignment of greater than 100 sequences must be done using a computer.

As discussed above, the specification also states “[t]he method of the invention also makes it possible to construct a database which constitutes a decision-making tool[.]” *See e.g.* paragraph [0069] of the originally filed application (emphasis added). One of ordinary skill in the art would recognize that such a database is a computer database. In fact, this is consistent with a reasonable interpretation of the term “database” in the context of the application to mean “any electronically-stored collection of data.” *See e.g.* Alan Freedman, The Computer Glossary 90 (8th Ed. 1998). Furthermore, Example 1 clearly shows the output from the claimed methods to a computer controlled display such as a computer controlled display screen or computer controlled printer.

Most importantly, the Patent Office itself recognized that the application and claimed subject matter relates to “apparatus and corresponding methods” utilizing a “data processing system or calculating computer” when it classified this claimed subject matter and application as belonging to US Classification 702/20. The International Classification G06F 19/00 assigned to the claimed subject matter and application also supports this conclusion. This is because International Classification G06F 19/00 is directed to digital computing, data processing equipment and methods adapted for specific applications.

This conclusion is also consistent with the Declaration of Sophie Brouillet made under 37 CFR §1.132 and previously made of record. *See* Declaration of Sophie Brouillet under 37 CFR

§1.132 (comments concerning CLUSTAL W algorithm and technological field of the art). It should also be noted again that the recitation of “outputting the identified motifs to a computer controlled display” is consistent with the Examiner’s helpful guidance in both the current Official Action mailed November 19, 2008 and the previous Official Action mailed February 19, 2008.

Thus, the foregoing makes it clear one of ordinary skill in the art would recognize the claimed methods are performed using at least one specifically programmed computer capable of executing the steps of the method and outputting the identified motifs to a computer controlled display.

The Applicants respectfully request the withdrawal of the rejections of Claims 1-10, 20 and 28-29 under 35 USC §112, first paragraph.

Claims 1-10, 20 and 28-29 are rejected as obvious under 35 USC §103(a) over the combination of Rose and Zhang.

Claims 1-10, 20 and 28-29 are not obvious under 35 USC §103(a) over the combination of Rose and Zhang. Reasons are set forth below.

Rose appears to describe a program named HYPERMUT which merely takes a multiple nucleotide sequence alignment and “compares every sequence in an alignment to the first sequence.” See Rose at 401. The HYPERMUT program then “identifies the changes [and], compares them with neighboring locations in the reference sequence.” Importantly, Rose does not describe the step of “identifying motifs not having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set” as recited in Claim 1. Rose does not describe the construction of all the matrices of Claim 6 such as NONMUTATED MATRIX B or MUTATED MATRIX C. Rose does not describe outputting the identified motifs (e.g. those identified via NONMUTATED MATRIX B or MUTATED MATRIX C) to a computer controlled display.

Zhang appears to describe the isolation and characterization of HIV-1 variants from patients followed by conventional sequence analyses. In Zhang these conventional sequence analyses merely describe the multiple sequence alignment of the *env* gene sequences from the HIV variants isolated from the patients using a CLUSTAL algorithm followed by the creation of a sequence identity based phylogenetic tree to describe the sequence divergence and “relatedness” between these sequences. Zhang also does not describe the step of “identifying

motifs not having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set” as recited in Claim 1. Zhang also does not describe the construction of all the matrices of Claim 6 such as NONMUTATED MATRIX B or MUTATED MATRIX C. Zhang also does not describe outputting the identified motifs (*e.g.* those identified via NONMUTATED MATRIX B or MUTATED MATRIX C) to a computer controlled display.

Thus, the combination of Rose and Zhang fails to teach all the elements of the claimed methods. This means one of ordinary skill in the art would not be motivated to combine Rose and Zhang or have a reasonable expectation of successfully so doing. Stated differently, the rejection fails to establish Claims 1-10, 20 and 28-29 are *prima facie* obvious under 35 USC §103(a) over the combination of Rose and Zhang.

The Applicants respectfully request the withdrawal of the rejection of Claims 1-10, 20 and 28-29 as obvious under 35 USC §103(a) over the combination of Rose and Zhang.

Claims 3 and 6-8 are rejected as obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins.

Claims 3 and 6-8 are not obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins. Reasons are set forth below.

The deficiencies of the core combination of Rose and Zhang, which fails to teach all the elements of Claims 3 and 6-8, are as discussed above. Collins does nothing to correct the deficiencies of this core combination of references. This is because Collins is merely concerned with constructing multiple sequence alignments and pairwise alignments for use in computer sequence database queries. Furthermore, the matrices shown in Collins are merely constructed for the purpose of facilitating these alignments, and require different operations for their construction than the matrices of the claims. Additionally, any similarity between the matrices in Collins and the NONMUTATED MATRIX B or MUTATED MATRIX C is superficial. This is due to the fact that the notation used to describe matrices and the operations (*e.g.* Boolean logic) used for the construction of such matrices is relatively standard in the art.

Collins also does not describe the step of “identifying motifs not having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set” as recited in the claims. Collins also does not describe the construction of all the matrices of Claim 6 such as NONMUTATED MATRIX B or MUTATED

MATRIX C. Collins also does not describe outputting the identified motifs (*e.g.* those identified via NONMUTATED MATRIX B or MUTATED MATRIX C) to a computer controlled display as required by Claim 6 and the other claims.

Thus, the combination of Rose, Zhang and Collins fails to teach all the elements of the claimed methods. This means one of ordinary skill in the art would not be motivated to combine Rose, Zhang and Collins or have a reasonable expectation of successfully so doing. Stated differently, the rejection fails to establish Claims 3 and 6-8 are *prima facie* obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins.

The Applicants respectfully request the withdrawal of Claims 3 and 6-8 as obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins.

Claims 1-10, 20 and 28-29 have been provisionally rejected under 35 USC §101 as claiming the same invention as that of Claims 1-10, 21 and 29-30 of the copending application having Serial No. 11/480,014. The Applicants respectfully request that the provisional double-patenting rejection made under 35 USC §101 be held in abeyance until the identification of allowable subject matter.

In light of the foregoing, the Applicants respectfully submit that the entire application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



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